Disease Name — Tyrosinemia, type 1

Alternate name(s)	Hereditary infantile tyrosinemia, Hepatorenal tyrosinemia, Fumarylacetoacetase deficiency, Fumarylacetoacetate hydrolase
Acronym	FAH deficiency
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Tyrosinemia I chronic-type, Tyrosinemia II, Tyrosinemia III
Symptom onset	Infancy
Symptoms	Hepatocellular degeneration leading to acute hepatic failure or chronic cirrhosis and hepatocellular carcinoma, renal Fanconi syndrome, peripheral neuropathy, seizures and possible cardiomyopathy.
Natural history without treatment	Chronic liver disease leading to cirrhosis and hepatocellular carcinoma. Renal tubular disease (Fanconi syndrome) with phosphaturia, aminoaciduria and often glycosuria. May lead to clinical rickets. Peripheral neuropathy. Self-injurious behavior, seizures and cardiomyopathy have been observed. Coagulation problems.
Natural history with treatment	Hepatitic disease may progress despite dietary treatment. NTBC treatment leads to improvements in kidney, liver and neurologic function, but may not affect incidence of liver cancer.
Treatment	Dietary restriction of phenylalanine and tyrosine. NTBC (2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanedione) treatment which improves hepatic and renal function. Liver transplantation when indicated to prevent hepatocellular carcinoma. Vitamin D to heal rickets.
Other	Unpleasant odor due to accumulation of methionine. Sometimes described as “cabbage-like” odor.
Emergency Medical Treatment	See sheet from American College of Medical Genetics (attached) or for more information, go to websitehttp://www.acmg.net/StaticContent/ACT/Tyrosine.pdf
Physical phenotype	No abnormalities present at birth. May develop widely-spaced incisors, pes planus, epicanthus and microcephaly.
Inheritance	Autosomal recessive
General population incidence	1:100,000
Ethnic differences	Yes
Population	French Canadian (Saquency-Lac Saint Jean region) 1:20 carrier rate
Ethnic incidence	1:1846
Enzyme location	Liver, kidney, lymphocytes, fibroblasts
Enzyme Function	Metabolizes fumarylacetoacetic acid into fumaric acid and acetoacetic acid
Missing Enzyme	Fumarylacetoacetate hydrolase
Metabolite changes	Increased urinary succinylacetone, increased tyrosine and methionine in serum, increased alpha fetoprotein.
Prenatal testing	Enzymatic assay of amniocytes or CVS cells. Direct DNA testing in amniocytes or CVS cells if mutations known. Succinylacetone in amniotic fluid.
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=276700
Genetests Link	www.genetests.org
Support Group	National Urea Cycle Disorders Foundation http://www.nucdf.org National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/

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